

Lessons From Gattinoni

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Professor Luciano Gattinoni's contributions to critical care medicine transformed the management of ARDS and mechanical ventilation, shaping the foundation of modern intensive care. Among his landmark achievements, the so-called baby lung concept redefined ARDS as a condition characterized by reduced functional lung volume, rather than lung stiffness, leading to the development of lung-protective ventilation strategies that prioritize minimizing ventilator-induced lung injury. His work on positive end-expiratory pressure advanced the understanding of lung aeration, atelectasis, and recruitment, highlighting the role of CT imaging in respiratory research. His research on prone positioning elucidated its physiologic benefits and demonstrated its lifesaving potential for patients with severe ARDS, culminating in its widespread adoption. Additionally, his work on mechanical power provided a unifying framework for assessing ventilator-induced lung injury risk, although challenges in its bedside application remain. Through his relentless pursuit of integrating respiratory physiology into clinical practice, Professor Gattinoni inspired generations of clinicians and researchers, leaving an indelible legacy that continues to guide advancements in critical care worldwide. CHEST Critical Care 2025; 3(2):100153

KEY WORDS: ARDS; ECLS; Gattinoni; mechanical ventilation; physiology

The critical care community experienced a profound loss with the recent passing of Professor Luciano Gattinoni. His pioneering contributions to the management of ARDS and mechanical ventilation greatly advanced the understanding of respiratory physiology, shaping modern intensive care practices and inspiring generations of clinicians and researchers worldwide. His work will continue to guide the practice and innovation of critical care medicine for years to come.

A defining element of Professor Gattinoni's legacy was his transformative approach to mechanical ventilation, shifting the focus from optimizing gas exchange to reducing the risk of ventilator-induced lung injury (VILI). Together with his colleagues, he emphasized the importance of integrating physiology into clinical decision-making, introducing key concepts such as lung protection and lung rest. He advocated for ventilation strategies that prioritized lung recovery, emphasizing that ventilatory tools should be used judiciously to minimize

ABBREVIATIONS: ECCO₂R = extracorporeal CO₂ removal; ECMO = extracorporeal membrane oxygenation; MP = mechanical power; PEEP = positive end-expiratory pressure; VILI = ventilator-induced lung injury; V_T = tidal volume

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DOI: <https://doi.org/10.1016/j.chstcc.2025.100153>

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harm. His work on extracorporeal techniques, including extracorporeal CO₂ removal (ECCO₂R), set the stage for modern advancements in extracorporeal respiratory support.

Beyond his scientific achievements, Professor Gattinoni was known for challenging assumptions, pushing the boundaries of conventional thinking, and seeking new ways to understand the pathophysiologic characteristics of critical care syndromes. His research not only reshaped mechanical ventilation strategies, but also had a profound impact on patient care, improving outcomes and benefiting millions of critically ill patients worldwide.

The principles of lung protection and the risk reduction of VILI, once revolutionary, are now fundamental to mechanical ventilation, in large part because of Professor Gattinoni's contributions. This article honors his legacy by highlighting the key milestones of his career and summarizing his major contributions, as illustrated in Figure 1.

Legacy of Professor Luciano Gattinoni: Pioneering Advances in Critical Care

The Baby Lung

Professor Gattinoni introduced the baby lung concept in the mid 1980s,¹ providing a transformative understanding of ARDS. Based on pioneering research using CT imaging, Professor Gattinoni and his colleagues demonstrated that functional lung volume in ARDS is drastically reduced, comparable with that of an infant's lung.²⁻⁵ Before the introduction of the baby lung concept, it was widely believed that the lungs of patients with ARDS were stiff. However, Professor Gattinoni and

his colleagues demonstrated that the lungs were not stiff, but rather were reduced in size.

The baby lung paradigm shifted the focus of ventilatory management in ARDS from normalizing gas exchange to minimizing overdistension of the remaining functional lung tissue, prioritizing the risk reduction of VILI^{6,7} while maintaining adequate oxygenation and tolerating elevated levels of CO₂ (so-called permissive hypercapnia).^{8,9} This concept set the foundation for lung-protective ventilation strategies, such as the use of low tidal volumes and limiting plateau pressures, which remain central principles in ARDS management today.^{10,11}

Professor Gattinoni demonstrated that safe ventilation depends on reducing the risk excessive mechanical strain on the lung, which he quantified as the ratio of tidal volume (V_T) to functional lung volume. His team identified that physiologic strain should remain < 1 (where V_T equals the aerated lung's capacity) to avoid overdistension and subsequent injury. Furthermore, they identified that the specific elastance of the baby lung, that is, the pressure required to double its size at end expiration, is approximately 12.5 cm H₂O, a value consistent with healthy lungs.^{12,13} This insight provided a physiologic basis for determining safe transpulmonary pressures, helping clinicians to avoid excessive mechanical forces in the heterogeneous lung parenchyma characteristic of ARDS.

Professor Gattinoni's contributions extended beyond theory to practical changes in clinical care. The recognition that permissive hypercapnia and moderate hypoxemia are acceptable trade-offs when VILI is minimized represented a fundamental shift in ARDS. As he reflected, "as new knowledge progresses, old knowledge is abandoned or forgotten."¹⁴ Yet, the baby

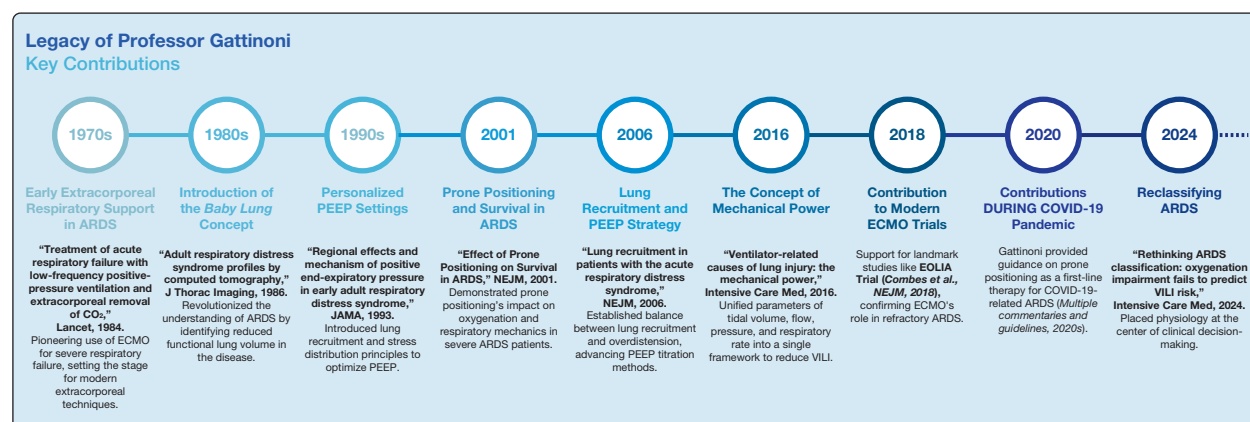


Figure 1 – Timeline showing the key contributions of Professor Luciano Gattinoni. ECMO = extracorporeal membrane oxygenation; EOLIA = Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome; PEEP = positive end-expiratory pressure; VILI = ventilator-induced lung injury. Created with [BioRender.com](https://www.biorender.com).

lung concept remains a cornerstone of critical care medicine, continuing to shape how clinicians understand and manage ARDS.

Physiologic Effects of Positive End-Expiratory Pressure and How to Set It

Professor Gattinoni led pivotal research into the physiologic effects of positive end-expiratory pressure (PEEP) and its optimal application in the management of ARDS. His work sought to address a critical balance: reducing the risk of alveolar collapse (atelectrauma) while avoiding overdistension (volutrauma). Through CT imaging studies, Professor Gattinoni and his colleagues demonstrated that PEEP could reduce the coexistence of atelectrauma and volutrauma by recruiting previously collapsed alveoli while promoting a more homogeneous distribution of mechanical forces across the lung.^{5,13,15,16}

Professor Gattinoni's research introduced the concept of *recruitability*, highlighting the heterogeneity of lung collapse in ARDS and the need to tailor PEEP settings to individual lung physiology.¹⁷ By using CT scans, his team quantified the potential for lung recruitment and demonstrated that the application of PEEP should be guided by the patient's specific degree of recruitable lung tissue. Their data showed for the first time that the use of higher PEEP levels in patients with a lower percentage of potentially recruitable lung provides little benefit and may even be harmful. Gattinoni's work emphasized that PEEP not only should improve oxygenation, but also should minimize VILI,¹³ advocating for an approach that considers both recruitment potential and the risk of overdistension.

Although no universally accepted method for personalizing PEEP has been established, his research provided a physiologic framework that continues to inform clinical strategies. The recognition of lung heterogeneity and the dynamic nature of recruitment has shaped contemporary approaches to PEEP titration, which now are integrated into evidence-based ARDS management guidelines.^{18,19}

Prone Positioning in ARDS: Physiologic and Clinical Implications

The prone position remains a cornerstone of care for severe ARDS, reflecting Professor Gattinoni's dedication to advancing our understanding of its physiologic and clinical implications. The therapeutic use of the prone position in acute respiratory failure was noted first in 1976, when it was reported to improve oxygenation in

patients.²⁰ Since then, extensive research, including animal models and clinical studies, has elucidated the physiologic benefits of this intervention. By redistributing lung aeration, it increases end-expiratory lung volume and reduces dorsal atelectasis, leading to improved ventilation/perfusion ($\dot{V}/\dot{Q}$) matching.^{21,22} This redistribution also promotes more uniform ventilation, alleviating both regional overdistension and atelectasis, 2 key contributors to VILI.²³⁻²⁷ Additionally, prone positioning optimizes chest wall mechanics, decreasing the pleural pressure gradient and leading to a more homogeneous transpulmonary pressure distribution. This, in turn, reduces the pressure load on the diaphragm, enhances its function, and further supports oxygenation and lung protection.²⁸ Collectively, these effects help to minimize mechanical stress on the heterogeneous lung parenchyma characteristic of ARDS.

In 2001, Professor Gattinoni led the first randomized controlled trial assessing the impact of prone positioning on survival in acute respiratory failure.²⁹ Although this trial and subsequent studies demonstrated significant oxygenation improvements, they failed to show a survival benefit.³⁰⁻³² However, meta-analyses³³⁻³⁵ later revealed that prone positioning significantly reduces mortality in patients with severe ARDS, particularly those with PaO_2 to FiO_2 ratio of < 150 . These findings paved the way for the landmark Prone Positioning in Severe Acute Respiratory Distress Syndrome (PROSEVA) trial,³⁶ which confirmed a substantial reduction in mortality in this population, cementing prone positioning as a standard-of-care intervention.

Professor Gattinoni's work in this area provided crucial physiologic insights that helped to refine the clinical application of prone positioning. His research contributed to a deeper understanding of both benefits and limitations,^{37,38} reinforcing the importance of integrating physiologic principles into clinical practices, a lesson that continues to inspire advancements in critical care today.

Mechanical Power: a Unifying Metric for Ventilator-Induced Lung Injury

In 2016, Gattinoni and colleagues³⁹ introduced mechanical power (MP) as a framework to unify key ventilator parameters implicated in the development of VILI, including $\dot{V}_T$, pressure, flow, resistance, and respiratory rate (Table 1). MP is defined as the total energy transferred by the ventilator to the respiratory system over time, calculated by multiplying the classical

TABLE 1] Mathematical Equations for Bedside Mechanical Power Calculation

Ventilation Mode	Equation	Advantages
Volume controlled	$MP = \{V_T^2 \times (1/2 \times E_{RS} + RR \times (1 + I/E) / (60 \times I/E) \times R_{RS}) + V_T \times PEEP\} \times RR \times 0.098^{39}$ $MP = V_T \times (P_{peak} - (\Delta P) / 2) \times RR \times 0.098^{39}$	- Validated in ARDS and normal lungs - Simplified MP equation - Easy to calculate without inspiratory hold - Validated in ARDS and normal lungs
Pressure controlled	$MP = V_T \times (\Delta P_{dyn} + PEEP) \times RR \times 0.098^{41}$	- Allows breath-by-breath monitoring - No inspiratory hold required
Dynamic (all modes)	$MP_{dyn} = V_T \times (P_{peak} - (\Delta P_{dyn}) / 2) \times RR \times 0.098^{42}$	- Suitable for all ventilation modes - Enables continuous VILI risk assessment

Summary of simplified equations for calculating mechanical power at the bedside. The simplified equation offers a practical and robust option for most clinical scenarios, enabling bedside assessment of mechanical power without requiring inspiratory or expiratory holds. Key assumptions include constant airway resistance (R_{RS}) and linear compliance (C_{RS}) during inspiration. ΔP = driving pressure ($P_{plat} - PEEP$); ΔP_{dyn} = dynamic driving pressure ($P_{peak} - PEEP$); E_{RS} = elastance of the respiratory system; I/E = inspiratory to expiratory time ratio; MP = mechanical power; MP_{dyn} = dynamic mechanical power; PEEP = positive end-expiratory pressure; P_{plat} = plateau pressure; P_{peak} = peak inspiratory pressure; RR = respiratory rate; R_{RS} = resistance of the respiratory system; VILI = ventilator-induced lung injury; V_T = tidal volume.

equation of motion by V_T and respiratory rate.³⁹ This metric provided a broader perspective on the mechanical forces contributing to lung injury and reinforced the importance of limiting ventilatory energy transfer to minimize harm.⁴⁰

Although studies have shown that higher MP is associated with worse outcomes in patients with ARDS,^{43–47} its clinical application remains limited. Challenges include the complexity of its calculation, a lack of consensus on the optimal equation, and the absence of a universally accepted threshold to guide practice.⁴⁸ Furthermore, MP's reliance on global parameters such as respiratory system elastance and airway resistance may not reflect fully local lung mechanics or the heterogeneity of lung injury. Simplified formulas—particularly in volume-controlled ventilation—correlate well with the original equation, but assume constant flow, airway resistance, and linear respiratory system compliance throughout inspiration, which limit their precision in diverse clinical scenarios.^{49,50}

Interestingly, although MP offers a holistic approach to assessing VILI risk, studies suggest that simpler variables, such as driving pressure, V_T , or respiratory rate, may predict outcomes with similar accuracy.⁵¹ Nevertheless, the concept of MP has enriched our understanding of lung protection by providing a framework that integrates the interplay of multiple factors, emphasizing the cumulative nature of ventilator-induced energy transfer.

As dynamic MP⁴² (ie, a simplified MP formula using dynamic driving pressure represented as [peak inspiratory pressure – PEEP]) evolves as a practical,

continuous metric for evaluating VILI risk, further research is needed to refine its application (Table 1). Although its clinical usefulness remains debated, MP represents an extension of Professor Gattinoni's legacy in exploring novel ways to understand and quantify mechanical ventilation's impact on the lung.

Extracorporeal Respiratory Support: The Tool to Buy Time

Professor Gattinoni was a pioneer in advocating for the use of extracorporeal techniques such as ECCO₂R and extracorporeal membrane oxygenation (ECMO) in the early management of ARDS.^{52–55} His research contributed to a deeper understanding of how extracorporeal respiratory support could mitigate the deleterious effects of mechanical ventilation and provide an opportunity for the lungs to heal.

Early in his career, Professor Gattinoni participated in foundational studies evaluating the role of extracorporeal support in ARDS.^{56–59} Although initial trials, including the multicenter randomized controlled trial led by Zapol and colleagues,⁶⁰ yielded disappointing results and raised doubts about the efficacy of ECMO in ARDS, Professor Gattinoni shifted focus toward alternative approaches. He proposed that ECCO₂R, combined with significantly reduced ventilation settings—sometimes as low as 2 to 3 breaths/min—could help to protect the lungs from barotrauma and volutrauma.⁵⁹ This strategy aimed to maintain oxygenation via diffusion through the native lungs while reducing the damaging effects of high-pressure, high-volume ventilation.

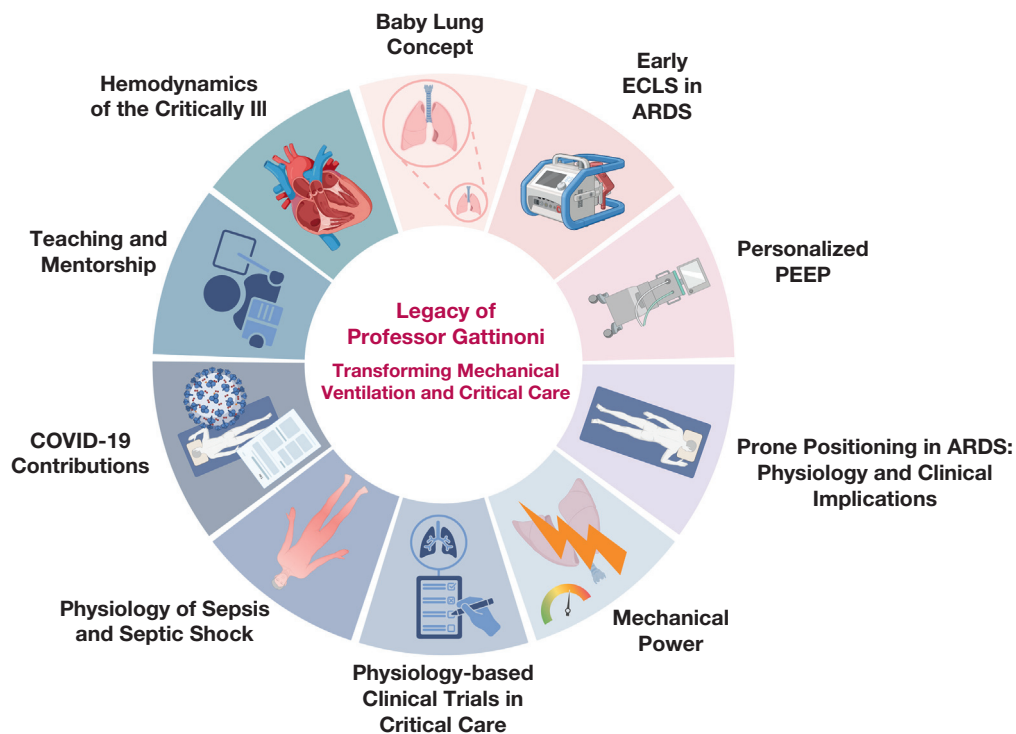


Figure 2 – Diagram showing the key contributions of Professor Luciano Gattinoni: advancing knowledge in the critical care. His legacy encompasses groundbreaking concepts such as the baby lung in ARDS, the physiologic basis for prone positioning, and early implementation of ECLS. He championed personalized approaches to mechanical ventilation, including the use of individualized PEEP and the importance of minimizing mechanical power to reduce ventilator-induced lung injury. Beyond ARDS and ventilation, his work extended to the hemodynamics of critically ill patients, sepsis physiologic characteristics, and COVID-19 management. Professor Gattinoni's influence also shaped clinical trial design, emphasizing physiology-based interventions, and his dedication to teaching and mentorship inspired a generation of intensivists worldwide. ECLS = extracorporeal life support; PEEP = positive end-expiratory pressure. Created with [BioRender.com](https://www.biorender.com).

Professor Gattinoni's work contributed to the ongoing re-evaluation of the role of ECMO in ARDS. Over the years, clinical trials have struggled to demonstrate statistically significant survival benefits consistently for ECMO. Notably, the Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA) trial⁶¹ was halted for futility; however, its findings were interpreted as a so-called positive negative trial, reflecting a shift in the perception of ECMO's value. Despite the lack of definitive evidence from randomized controlled trials, Professor Gattinoni emphasized ECMO's role as a tool to buy time until disease resolution, a conviction grounded in clinical experience, rather than statistical outcomes.⁶²

Similarly, ECCO₂R emerged as a complementary approach, particularly in cases of less severe ARDS. By facilitating ultraprotective ventilation strategies, ECCO₂R allowed for further reductions in V_T s and driving pressures, thus further limiting VILI.^{63,64} Professor Gattinoni envisioned that simpler vascular access, akin to that used in renal dialysis, could make ECCO₂R a more accessible option, even in earlier stages of ARDS.⁵⁹

Professor Gattinoni's advocacy for extracorporeal techniques highlighted their potential not only to improve gas exchange, but also to create a more favorable environment for lung recovery.⁶² He underscored the importance of considering factors beyond gas exchange, such as lung compliance and the systemic effects of high-pressure ventilation, when determining the appropriate timing and indications for ECMO and ECCO₂R.^{62,65}

Conclusions

This review highlights just a few of Professor Gattinoni's key contributions, but his legacy extends far beyond, with > 600 peer-reviewed articles covering a broad spectrum of topics, including sepsis, acid-base balance, hemodynamics, advanced imaging techniques, and more, in critically ill patients (Fig 2). From his groundbreaking work on the baby lung concept to his leadership in prone positioning and ECMO, his visionary ideas have reshaped modern ARDS management, directly impacting clinical practices and patient outcomes. His work will continue to inspire new

generations of researchers and drive advancements that will shape the future of mechanical ventilation and intensive care medicine for years to come.

Funding/Support

B. P. receives funding from the National Heart, Lung, and Blood Institute, National Institutes of Health (Grants K23HL148387 and U01HL168308).

Financial/Nonfinancial Disclosures

The authors have reported to *CHEST Critical Care* the following: E. F. reports personal fees from Aerogen, Baxter, Boehringer Ingelheim, Getinge, Inspira, Mallinckrodt, and Vasomune outside the submitted work. None declared (A. C.-F., T. P., B. P.).

Acknowledgments

Author contributions: E. F. conceived the idea for this tribute piece. A. C.-F. drafted the first version of the manuscript. T. P., B. P., and E. F. contributed to the writing and revision of the manuscript. All authors reviewed and approved the final version.

Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

References

- Gattinoni L, Pesenti A. ARDS: the non-homogeneous lung; facts and hypothesis. *Intensive Crit Care Digest*. 1987;6(1):1-4.
- Rommelsheim K, Lackner K, Westhofen P, Distelmaier W, Hirt S. Respiratory distress syndrome of the adult in the computer tomograph [in German]. *Anasth Intensivther Notfallmed*. 1983;18(2):59-64.
- Maunder RJ, Shuman WP, McHugh JW, Marglin SI, Butler J. Preservation of normal lung regions in the adult respiratory distress syndrome: analysis by computed tomography. *JAMA*. 1986;255(18):2463-2465.
- Gattinoni L, Mascheroni D, Torresin A, et al. Morphological response to positive end expiratory pressure in acute respiratory failure. Computerized tomography study. *Intensive Care Med*. 1986;12(3):137-142.
- Gattinoni L, Caironi P, Pelosi P, Goodman LR. What has computed tomography taught us about the acute respiratory distress syndrome? *Am J Respir Crit Care Med*. 2001;164(9):1701-1711.
- Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2013;369(22):2126-2136.
- Gattinoni L, Carlesso E, Cadringer P, Valenza F, Vagginielli F, Chiumello D. Physical and biological triggers of ventilator-induced lung injury and its prevention. *Eur Respir J Suppl*. 2003;47:15s-25s.
- Hickling KG, Henderson SJ, Jackson R. Low mortality associated with low volume pressure limited ventilation with permissive hypercapnia in severe adult respiratory distress syndrome. *Intensive Care Med*. 1990;16(6):372-377.
- Pesenti A. Target blood gases during ARDS ventilatory management. *Intensive Care Med*. 1990;16(6):349-351.
- Qadir N, Sahetya S, Munshi L, et al. An update on management of adult patients with acute respiratory distress syndrome: an official American Thoracic Society clinical Practice guideline. *Am J Respir Crit Care Med*. 2024;209(1):24-36.
- The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301-1308.
- Gattinoni L, Pesenti A, Avalli L, Rossi F, Bombino M. Pressure-volume curve of total respiratory system in acute respiratory failure. Computed tomographic scan study. *Am Rev Respir Dis*. 1987;136(3):730-736.
- Gattinoni L, D'andrea L, Pelosi P, Vitale G, Pesenti A, Fumagalli R. Regional effects and mechanism of positive end-expiratory pressure in early adult respiratory distress syndrome. *JAMA*. 1993;269(16):2122-2127.
- Gattinoni L, Pesenti A. The concept of "baby lung." *Intensive Care Med*. 2005;31(6):776-784.
- Gattinoni L, Pesenti A, Bombino M, et al. Relationships between lung computed tomographic density, gas exchange, and PEEP in acute respiratory failure. *Anesthesiology*. 1988;69(6):824-832.
- Gattinoni L, Pelosi P, Crotti S, Valenza F. Effects of positive end-expiratory pressure on regional distribution of tidal volume and recruitment in adult respiratory distress syndrome. *Am J Respir Crit Care Med*. 1995;151(6):1807-1814.
- Gattinoni L, Caironi P, Cressoni M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. *N Engl J Med*. 2006;354(17):1775-1786.
- Pelosi P, Ball L, Barbas CSV, et al. Personalized mechanical ventilation in acute respiratory distress syndrome. *Crit Care*. 2021;25(1):250.
- Taenaka H, Yoshida T, Hashimoto H, et al. Personalized ventilatory strategy based on lung recruitability in COVID-19-associated acute respiratory distress syndrome: a prospective clinical study. *Crit Care*. 2023;27(1):152.
- Piehl MA, Brown RS. Use of extreme position changes in acute respiratory failure. *Crit Care Med*. 1976;4(1):13-14.
- Pappert D, Rossaint R, Sлама K, Gruning T, Falke KJ. Influence of positioning on ventilation-perfusion relationships in severe adult respiratory distress syndrome. *Chest*. 1994;106(5):1511-1516.
- Douglas WW, Rehder K, Beynen FM, Sessler AD, Marsh HM. Improved oxygenation in patients with acute respiratory failure: the prone position. *Am Rev Respir Dis*. 1977;115(4):559-566.
- Broccard A, Shapiro RS, Schmitz LL, Adams AB, Nahum A, Marini JJ. Prone positioning attenuates and redistributes ventilator-induced lung injury in dogs. *Crit Care Med*. 2000;28(2):295-303.
- Mentzelopoulos SD, Roussos C, Zakynthinos SG. Prone position reduces lung stress and strain in severe acute respiratory distress syndrome. *Eur Respir J*. 2005;25(3):534-544.
- Galiatsou E, Kostanti E, Svarna E, et al. Prone position augments recruitment and prevents alveolar overinflation in acute lung injury. *Am J Respir Crit Care Med*. 2006;174(2):187-197.
- Papazian L, Gainnier M, Marin V, et al. Comparison of prone positioning and high-frequency oscillatory ventilation in patients with acute respiratory distress syndrome. *Crit Care Med*. 2005;33(10):2162-2171.
- Pelosi P, Tubiolo D, Mascheroni D, et al. Effects of the prone position on respiratory mechanics and gas exchange during acute lung injury. *Am J Respir Crit Care Med*. 1998;157(2):387-393.
- Albert RK, Leasa D, Sanderson M, Robertson HT, Hlastala MP. The prone position improves arterial oxygenation and reduces shunt in oleic-acid-induced acute lung injury. *Am Rev Respir Dis*. 1987;135(3):628-633.
- Gattinoni L, Tognoni G, Pesenti A, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med*. 2001;345(8):568-573.
- Guerin C, Gaillard S, Lemasson S, et al. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. *JAMA*. 2004;292(19):2379-2387.
- Mancebo J, Fernández R, Blanch L, et al. A multicenter trial of prolonged prone ventilation in severe acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2006;173(11):1233-1239.
- Taccone P, Pesenti A, Latini R, et al. Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2009;302(18):1977-1984.
- Gattinoni L, Carlesso E, Taccone P, Polli F, Guérin C, Mancebo J. Prone positioning improves survival in severe ARDS: a

pathophysiologic review and individual patient meta-analysis. *Minerva Anestesiol.* 2010;76(6):448-454.

34. Sud S, Friedrich JO, Taccone P, et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. *Intensive Care Med.* 2010;36(4):585-599.
35. Abroug F, Ouannes-Besbes L, Elatrous S, Brochard L. The effect of prone positioning in acute respiratory distress syndrome or acute lung injury: a meta-analysis. Areas of uncertainty and recommendations for research. *Intensive Care Med.* 2008;34(6):1002-1011.
36. Guérin C, Reigner J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med.* 2013;368(23):2159-2168.
37. Pelosi P, Brazzi L, Gattinoni L. Prone position in acute respiratory distress syndrome. *Eur Respir J.* 2002;20(4):1017-1028.
38. Gattinoni L, Taccone P, Carlesso E, Marini JJ. Prone position in acute respiratory distress syndrome rationale, indications, and limits. *Am J Respir Crit Care Med.* 2013;188(11):1286-1293.
39. Gattinoni L, Tonetti T, Cressoni M, et al. Ventilator-related causes of lung injury: the mechanical power. *Intensive Care Med.* 2016;42(10):1567-1575.
40. Cressoni M, Gotti M, Chiurazzi C, et al. Mechanical power and development of ventilator-induced Lung Injury. *Anesthesiology.* 2016;124(5):1100-1108.
41. Becher T, van der Staay M, Schädler D, Frerichs I, Weiler N. Calculation of mechanical power for pressure-controlled ventilation. *Intensive Care Med.* 2019;45(9):1321-1323.
42. Urner M, Jüni P, Hansen B, Wettstein MS, Ferguson ND, Fan E. Time-varying intensity of mechanical ventilation and mortality in patients with acute respiratory failure: a registry-based, prospective cohort study. *Lancet Respir Med.* 2020;8(9):905-913.
43. Guérin C, Papazian L, Reigner J, Ayzac L, Loundou A, Forel JM. Effect of driving pressure on mortality in ARDS patients during lung protective mechanical ventilation in two randomized controlled trials. *Crit Care.* 2016;20(1):384.
44. Serpa Neto A, Deliberato RO, Johnson AEW, et al. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. *Intensive Care Med.* 2018;44(11):1914-1922.
45. Parhar KKS, Zjadewicz K, Soo A, et al. Epidemiology, mechanical power, and 3-year outcomes in acute respiratory distress syndrome patients using standardized screening. An observational cohort study. *Ann Am Thorac Soc.* 2019;16(10):1263-1272.
46. Costa ELV, Slutsky AS, Brochard LJ, et al. Ventilatory variables and mechanical power in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2021;204(3):303-311.
47. Van Meenen DMP, Algera AG, Schuijt MTU, et al. Effect of mechanical power on mortality in invasively ventilated ICU patients without the acute respiratory distress syndrome: an analysis of three randomised clinical trials. *Eur J Anaesthesiol.* 2023;40(1):21-28.
48. von Düring S, Parhar KKS, Adhikari NKJ, et al. Understanding ventilator-induced lung injury: the role of mechanical power. *J Crit Care.* 2025;85:154902.
49. Giosa L, Busana M, Pasticci I, et al. Mechanical power at a glance: a simple surrogate for volume-controlled ventilation. *Intensive Care Med Exp.* 2019;7(1):61.
50. Chiumello D, Gotti M, Guanziroli M, et al. Bedside calculation of mechanical power during volume- and pressure-controlled mechanical ventilation. *Crit Care.* 2020;24(1):417.
51. Dianti J, Matelski J, Tisminetzky M, et al. Comparing the effects of tidal volume, driving pressure, and mechanical power on mortality in trials of lung-protective mechanical ventilation. *Respir Care.* 2021;66(2):221-227.
52. Fan E, Gattinoni L, Combes A, et al. Venovenous extracorporeal membrane oxygenation for acute respiratory failure: a clinical review from an international group of experts. *Intensive Care Med.* 2016;42(5):712-724.
53. Chiumello D, Brochard L, Marini JJ, et al. Respiratory support in patients with acute respiratory distress syndrome: an expert opinion. *Crit Care.* 2017;21(1):240.
54. Gattinoni L, Vassalli F, Romitti F, et al. Extracorporeal gas exchange: when to start and how to end? *Crit Care.* 2019;23(suppl 1):203.
55. Quintel M, Bartlett RH, Grocott MPW, et al. Extracorporeal membrane oxygenation for respiratory failure. *Anesthesiology.* 2020;132(5):1257-1276.
56. Kolobow T, Gattinoni L, Tomlinson TAJE. Control of breathing using an extracorporeal membrane lung. *Anesthesiology.* 1977;46(2):138-141.
57. Gattinoni L, Kolobow T, Tomlinson T, et al. Low-frequency positive pressure ventilation with extracorporeal carbon dioxide removal (LFPPV-ECCO2R): an experimental study. *Anesth Analg.* 1978;57(4):470-477.
58. Kolobow T, Pesenti A, Solca ME, Gattinoni L. A new approach to the prevention and treatment of acute pulmonary insufficiency. *Int J Artif Organs.* 1980;3(2):86-93.
59. Gattinoni L, Pesenti A, Rossi GP, et al. Treatment of acute respiratory failure with low-frequency positive-pressure ventilation and extracorporeal removal of CO₂. *Lancet.* 1980;2(8189):292-294.
60. Zapol WM, Snider MT, Hill JD, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. *JAMA.* 1979;242(20):2193-2196.
61. Combes A, Hajage D, Capellier G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med.* 2018;378(21):1965-1975.
62. Gattinoni L. Definitions, guidelines and opinions: the white, the black and the grey. *Intensive Care Med.* 2024;50(6):934-936.
63. Duscio E, Cipulli F, Vasques F, et al. Extracorporeal CO₂ removal: the minimally invasive approach, theory, and practice. *Crit Care Med.* 2019;47(1):33-40.
64. Chiumello D, Pozzi T, Mereto E, et al. Long term feasibility of ultraprotective lung ventilation with low-flow extracorporeal carbon dioxide removal in ARDS patients. *J Crit Care.* 2022;71:154092.
65. Catozzi G, Pozzi T, Nocera D, et al. Rethinking ARDS classification: oxygenation impairment fails to predict VILI risk. *Intensive Care Med.* 2025;51(1):62-71.